Medical Staff Conference

Therapeutic Options in the Management of Life-Threatening Arrhythmias

Discussants
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These discussions are selected from the weekly staff conferences in the Department of Medicine, University of California, San Francisco. Taken from transcriptions, they are prepared by Homer A. Boushey, MD, Professor of Medicine, and John G. Fitz, MD, Assistant Professor of Medicine, under the direction of Lloyd H. Smith, Jr, MD, Professor of Medicine and Associate Dean in the School of Medicine. Requests for reprints should be sent to the Department of Medicine, University of California, San Francisco, School of Medicine, San Francisco, CA 94143.

RICHARD K. ROOT, MD*: *In the past decade great advances have occurred in the diagnosis and treatment of life-threatening arrhythmias. It is becoming increasingly possible to tailor individual therapy, rather than simply to rely on trials of antiarrhythmic drugs. The principles underlying this evolving approach to cardiac arrhythmias will be reviewed by Drs Herre and Griffin of the Electrophysiology Section in the Division of Cardiology.*

JOHN M. HERRE, MD†: The development of newer antiarrhythmic drugs, surgical and catheter ablation techniques, antitachycardia pacemakers, and the automatic implantable cardioverter-defibrillator has allowed cardiac electrophysiologists to tailor therapy for the specific needs of a patient, taking into consideration age, life-style, left ventricular function, previous responses to treatment, and patients' desires regarding treatment. To illustrate these options, we will present the following case.

Case Presentation

A 22-year-old man was referred to the cardiac electrophysiology service at the University of California, San Francisco (UCSF), because of recurrent, sustained ventricular tachycardia. He had been well until three years before admission when he first presented with sustained ventricular tachycardia at a rate of 180 per minute. The tachycardia was tolerated well and was terminated by elective, direct-current cardioversion. Over the subsequent three years, he was treated unsuccessfully with β-adrenergic blocking agents, procainamide hydrochloride, quinidine sulfate, and tocainide hydrochloride. His episodes of ventricular tachycardia resulted in numerous visits to emergency departments for cardioversion. On admission to UCSF, a physical examination revealed a grade II/VI murmur at the apex. No gallops were heard, and no other abnormalities were found.

A two-dimensional echocardiogram showed a 4-cm inferoseptal aneurysm with an overall ejection fraction of 0.45. Right- and left-sided filling pressures were normal, and coronary angiography showed normal coronary arteries. An electrophysiologic study was done. Sinus and atrioventricular node function was normal. Sustained ventricular tachycardia, identical in morphology and rate to the spontaneous tachycardia, was induced with two extrastimuli.

The treatment options available included the following:

- Further drug testing, including the use of amiodarone hydrochloride, guided by programmed ventricular stimulation.
- Antitachycardia pacing.
- Automatic implantable cardioverter-defibrillator.
- Catheter ablation.
- Map-guided aneurysmectomy and endocardial resection.

Programmed Ventricular Stimulation as a Method for Evaluating and Testing Therapy in Patients With Ventricular Tachycardia

The use of programmed ventricular stimulation to reproduce and evaluate therapy for ventricular tachycardia is based on experimental evidence that suggests that the mechanism for most recurrent sustained ventricular tachycardia is reentry at the border of a scar on the endocardial surface. In the vast majority of patients, the scar is caused by a myocardial infarction. The border zone consists of nonconducting scar tissue, normal myocardium, and abnormal but viable tissue. The tachycardia originates when the trigger, usually a premature ventricular beat, enters the border zone, finds one area refractory, and conducts slowly through abnormal myocardium. The slowed conduction allows the previously refractory area to recover by the time the wave front reaches it (Figure 1). As long as the wave front does not meet refractory tissue, the tachycardia persists. Antiarrhythmic agents may alter this substrate for ventricular tachycardia either by further slowing conduction or altering the refractoriness in such a way that reentry becomes impossible or cannot be sustained.

Programmed ventricular stimulation, by creating the trigger, provides electrophysiologists with a method for

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ABBREVIATIONS USED IN TEXT

AICD = automatic implantable cardioverter-defibrillator
UCSF = University of California, San Francisco

testing the effect of an antiarrhythmic agent on the substrate for reentry. One or more electrode catheters are advanced to the right ventricle from the femoral vein to provide pacing and to record from the endocardium.

Figure 2 shows the methods used in programmed ventricular stimulation. During normal sinus rhythm, a single premature extrastimulus (S2) is introduced at twice the current required to capture the ventricle in late diastole (Figure 2-A). If ventricular tachycardia is not induced, diastole is scanned until the extrastimulus fails to capture the ventricle (Figure 2-B). Next, two extrastimuli (S2 and S3) are introduced, and diastole is scanned again (Figure 2-C). Finally, as many as three extrastimuli may be introduced either during normal sinus rhythm or after a pacing train of six to eight beats at rates of 100 to 150 per minute. Figure 2-D shows the induction of a sustained ventricular tachycardia with the use of three extrastimuli (S2, S3, and S4) following an eight-beat train at a rate of 150 per minute. Because tachycardia induction may depend on the site of stimulation and on the rate of the train of pacing, extrastimulation is carried out at two or more sites and during sinus rhythm and after pacing trains at two or more rates. Because more aggressive pacing protocols may lead to the induction of nonclinical forms of tachycardia, more than three extrastimuli or higher pacing currents are not used in our laboratory.[1]

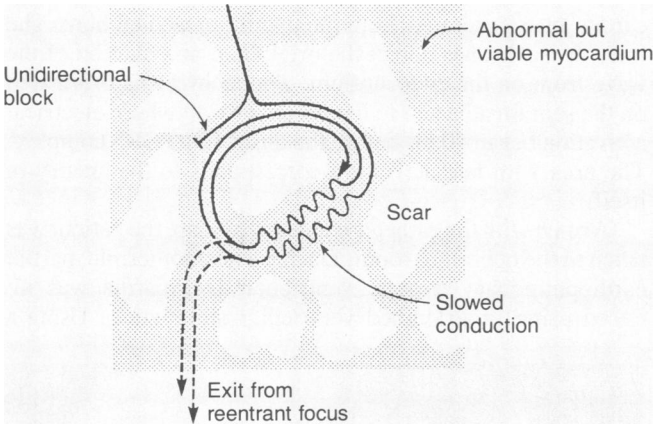

Figure 1.—The diagram shows the mechanism of reentry within an area of abnormal myocardium having heterogeneous conduction and patchy scarring. See text for details.

If ventricular tachycardia can be induced before but not after an antiarrhythmic agent is administered, then it is likely that the drug will prevent the spontaneous occurrence of the tachycardia.[2] If an induced tachycardia can be terminated reliably by pacing techniques or cardioversion-defibrillation, then it is likely that an automatic device will be successful. Finally, if the induced tachycardia is morphologically identical to the spontaneous arrhythmia and if the site of origin of the tachycardia can be located by mapping techniques, then catheter or surgical ablation is likely to prevent a recurrence of the tachycardia. Thus, the use of programmed ventricular stimulation is central to all of the options listed above.

Indications for Electrophysiologic Study in Patients With Ventricular Tachycardia

Because the likelihood of recurrence is so high, all patients resuscitated from cardiac arrest or who have had sustained ventricular tachycardia should undergo an electrophysiologic study for the selection of therapy. The high first-year mortality of patients following a myocardial infarction has led to an investigation of the use of electrophysiologic studies to evaluate the risk for sudden death in these patients. While some studies have suggested that electrophysiologic studies cannot differentiate between those patients likely to die suddenly and those likely to survive, recent studies from Australia have shown striking differences in survival between patients with and without inducible ventricular tachycardia.[3] Further studies will be needed before electrophysiologic studies can be recommended routinely following a myocardial infarction.

The usefulness of antiarrhythmic therapy for patients with asymptomatic, nonsustained ventricular tachycardia has been questioned. Electrophysiologic studies, by detecting those patients capable of sustained ventricular tachycardia, may allow an appropriate selection of patients for drug therapy. In a recent study by Gomes and co-workers, patients with good left ventricular function and no inducible sustained ventricular tachycardia had excellent prognoses compared with those with inducible ventricular tachycardia.[4] It has not yet been shown, however, that antiarrhythmic therapy alters the survival of such high-risk patients.

Finally, electrophysiologic study has been used to evaluate recurrent syncope. Particularly in patients with organic heart disease, ventricular tachycardia may cause syncope. The likelihood of a diagnostic study depends on the population studied and on the criteria used to define abnormal findings. Because these criteria vary greatly in the literature, the reported incidence of a diagnostic study ranges from 10% to

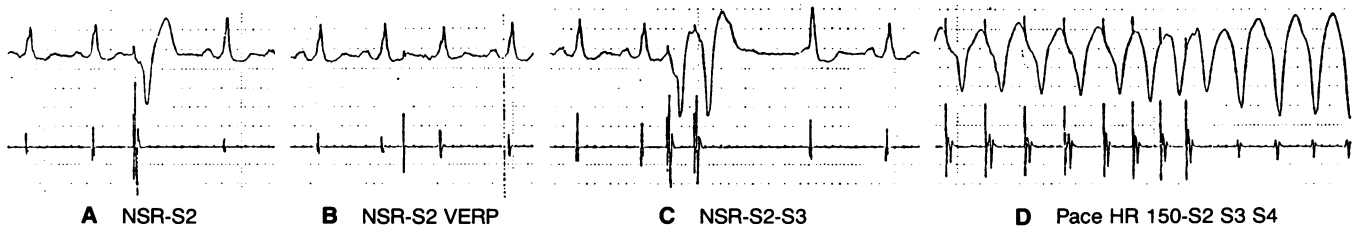

Figure 2.—These 4 panels illustrate the technique of programmed ventricular stimulation for arrhythmia induction. **A,** A single premature stimulus (S2) can be seen in both the surface electrocardiogram (top tracing) and the right ventricular endocardial electrogram (lower tracing). **B,** The premature stimulus is delivered at a cycle length sufficiently premature that it no longer is able to capture the ventricle, the ventricular effective refractory period (VERP). **C,** The initial stimulus interval has been increased just to the point of capture and a second premature stimulus (S3) added. **D,** Three premature extrastimuli are applied—S2, S3, and S4—following a period of ventricular pacing at a heart rate (HR) of 150 beats per minute. Ventricular tachycardia is seen following the last premature stimulus. NSR = normal sinus rhythm

83%.[5-7] The study is most useful in patients with organic heart disease, particularly a recent myocardial infarction, who have histories compatible with cardiac syncope and no abnormalities found on noninvasive and neurologic evaluations.

Approaches to the Treatment of Sustained Ventricular Arrhythmias

Drug Therapy

The treatment of recurrent sustained ventricular tachycardia can be approached in one of two ways. The trigger for sustained ventricular tachycardia can be attacked by attempting to eliminate or vastly reduce spontaneous ventricular premature beats, couplets, and nonsustained ventricular tachycardia observed on continuous or ambulatory monitoring. This method may be successful in patients with frequent spontaneous ventricular ectopic beats, which can be suppressed or eliminated by antiarrhythmic therapy. Many survivors of cardiac arrest, however, and patients with recurrent sustained ventricular tachycardia have only rare ventricular ectopy between episodes of sustained arrhythmia. These patients are not candidates for therapy based on ambulatory monitoring. The density of spontaneous ectopy and the degree of suppression required for a good result have not been established and validated.

Programmed ventricular stimulation allows an electrophysiologist to attack the substrate for arrhythmia. Most patients with ventricular tachycardia are treated with antiarrhythmic therapy. In general, following the induction of sustained ventricular tachycardia in a control (drug-free) state, procainamide is administered intravenously and programmed stimulation repeated. If ventricular tachycardia is rendered noninducible by intravenous procainamide, then oral procainamide or another class IA antiarrhythmic agent may be tried and programmed stimulation repeated after drug concentrations have been appropriately stabilized. If procainamide therapy fails, as it does frequently, a class IC drug such as flecainide, encainide, or propafenone or a class III drug such as sotalol (investigational) may be tried. Again, programmed stimulation is repeated after the drug level becomes stable. The trials of multiple drugs may be limited by a patient's left ventricular function. Drugs such as disopyramide, flecainide, and sotalol may worsen congestive heart failure. Drugs such as encainide and flecainide have a higher incidence of proarrhythmic effects when used in patients with poor left ventricular function.[8]

When trials of the above standard agents prove unsuccessful, amiodarone is used frequently. Its use is reserved for patients for whom other agents are unsuccessful or who are intolerant of other agents for several reasons. Because of its long half-life (about 60 days), antiarrhythmic effects are delayed, and if its use must be stopped because of ineffectiveness or intolerable side effects, elimination requires months. Side effects are common and tend to increase over time, making its use in younger patients problematic. Overall, amiodarone has little effect on left ventricular function and is frequently effective when all other agents have failed. Thus, it is used commonly in patients with poor left ventricular function and recurrent arrhythmias unresponsive to other agents.[9]

Recent evidence suggests that electrophysiologic studies may be useful in determining the prognosis of patients treated with amiodarone.[10,11] While tachycardia remains inducible in most patients, those with inducible but well-tolerated tachycardia have a better prognosis.

Despite the many antiarrhythmic agents available and the use of programmed stimulation to assess efficacy, recurrences of arrhythmia, sudden cardiac death, and intolerable side effects remain a significant problem. Fortunately, several approaches not dependent on pharmacologic therapy are now available. For the patient presented here, it seemed appropriate to pursue one of these nonpharmacologic options. The use of multiple drugs had failed clinically. With good left ventricular function and normal coronary arteries, long-term survival seemed likely if the arrhythmia could be controlled. Thus, treatment might have provided a short-term solution, but the likelihood of long-term side effects was prohibitive.

Catheter and Surgical Ablation of the Focus of Ventricular Tachycardia

To consider one of the ablative procedures, the focus of the tachycardia must be identified with sufficient precision to allow its destruction without compromising the integrity of the ventricles. This may be accomplished by ventricular mapping. In the electrophysiologic laboratory, several electrode catheters are advanced to the patient's right and left ventricles (Figure 3). The tachycardia is induced with programmed ventricular stimulation and the catheters moved about within the ventricles. Electrograms are recorded from each site and compared with the onset of the QRS complex on the surface electrocardiogram. The site where activation is earliest relative to the QRS complex is at or adjacent to the site of the origin of the tachycardia. Figure 4 shows an endocardial map generated from the patient presented here. The lines or isochrones depict the origin and propagation of the wave front on the endocardium. The tachycardia originated on the septum adjacent to the posterior wall where electrical activation began 40 ms before the onset of the QRS complex. The area with late activation corresponds to the aneurysm itself.

Armed with the catheter endocardial map, the patient was taken to the operating room. During a normothermic, partial cardiopulmonary bypass, ventricular tachycardia was induced using programmed ventricular stimulation. Using a

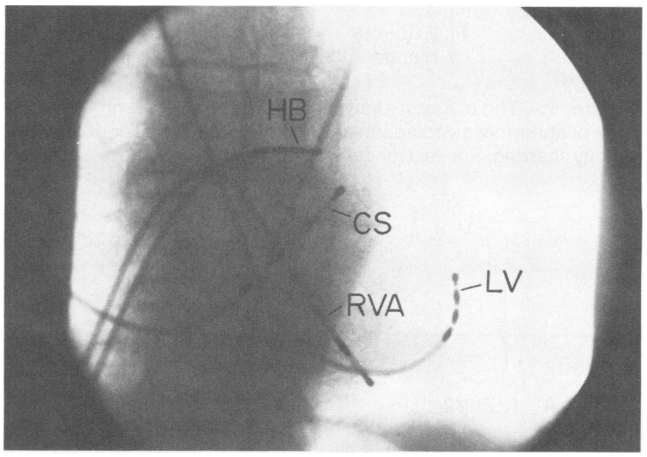

Figure 3.—The fluoroscopic image of the heart shows catheters placed for an electrophysiologic study and left ventricular mapping. Catheters are in place across the tricuspid valve near the bundle of His **(HB)**, in the coronary sinus **(CS)**, in the left ventricle **(LV)**, and in the right ventricular apex **(RVA)**.

hand-held bipolar electrode, electrograms were recorded from several epicardial sites. The isochronal map generated from the posterior portion of the heart is shown in Figure 5. Again, the site of earliest activation was adjacent to the aneurysm and corresponded to the site identified at the time of catheter mapping. Following the epicardial map, the ventricle was opened during ventricular tachycardia and the mapping repeated. The aneurysm and endocardium in the mapping-identified area of earliest activation were resected. Recently computers have been used to facilitate intraoperative mapping. Using plaques or socks with many electrodes, electrograms can be generated from many sites simultaneously, allowing complete maps to be generated from single beats during an episode of tachycardia. This significantly shortens the time required for mapping and allows mapping in patients with several morphologic types of tachycardia.

One week postoperatively, the patient was returned to the electrophysiologic laboratory and programmed ventricular stimulation repeated. Despite the use of three ventricular extrastimuli, no ventricular tachycardia could be induced. In our own and published experience, noninducibility following endocardial resection predicts an excellent outcome without the need for pharmacologic therapy. Overall results in the literature suggest an 80% success rate for endocardial resection.[12] Obviously, not all patients are candidates for open-heart operations, but endocardial resection affords an alternative to drug therapy for younger persons with preserved left ventricular function.

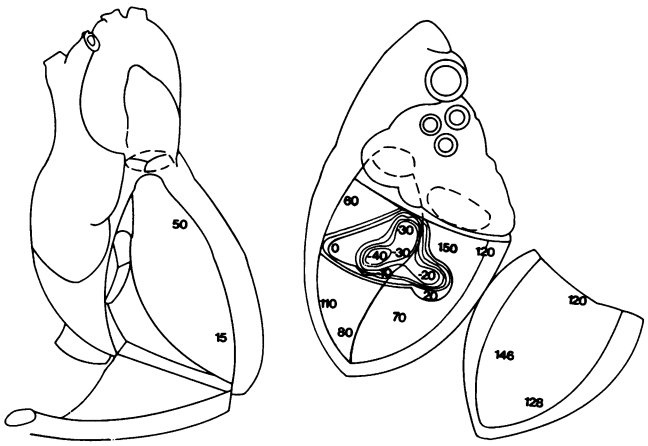

Figure 4.—The timing of activation of the endocardium is shown for both the right and left ventricles. The numbers identify isochrones of depolarization timed from the earliest beginning of a QRS complex in any standard surface electrocardiographic lead. The area of earliest activation is in the interventricular septum and occurs some 40 ms before the earliest surface Q wave.

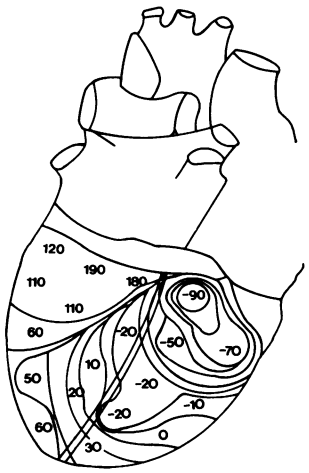

Figure 5.—This diagram shows the timing of activation of the epicardium as determined at the time of a surgical procedure. The view is of the posterior surface of the heart. The double line from base to apex represents the posterior descending coronary artery. The earliest activation occurs 90 ms before the earliest surface Q wave in an area adjacent to that identified on the endocardial map.

TABLE 1.—*Results of Catheter Ablation Worldwide**

Patients, No.	164
Follow-up duration, mo±SEM	12±11
Results	Patients, %
No ventricular tachycardia, no drugs	18
No ventricular tachycardia, taking drugs	41
Recurrent ventricular tachycardia, sudden death, or unsuccessful	34
Procedure-related deaths	7

SEM=standard error of the mean

*Data from the Percutaneous Cardiac Mapping and Ablation Registry.[16]

JERRY C. GRIFFIN, MD*: As Dr Herre mentioned, electrophysiologists, like their colleagues in the angiographic cardiovascular laboratories, have become far more interventional in the past five years. This is in large part due to ground-breaking work done here at UCSF in the early part of this decade by our colleague, Melvin Scheinman, MD. Dr Scheinman perfected the procedure now known as cardiac ablation, or fulguration.[13] The technique was originally used to block conduction at the atrioventricular junction to control the ventricular rate during a variety of atrial and supraventricular tachyarrhythmias. More recently it has been applied to foci of ventricular tachycardia and the accessory atrioventricular connections of the Wolff-Parkinson-White syndrome.[14,15] Although we are currently evaluating a number of other energy sources, including radio frequency and laser for the ablation of cardiac tissues, clinically we use the output of a standard defibrillator. This brief, high-voltage DC shock is applied either across the electrodes of a catheter inside the heart or from an electrode to a patch on the body surface. The first step in catheter ablation, as in surgical treatment, is to identify the site of earliest activation in the ventricles using mapping techniques. The center for the accumulation and maintenance of a National Institutes of Health multicenter international registry for catheter ablation for cardiac arrhythmias is here at UCSF. I will summarize the most recent compilation of that data, with regard to ventricular tachycardia.[16]

Data were obtained from 164 patients who had undergone catheter ablation of ventricular tachycardia. Most of the patients were men of early middle age. Although the predominant underlying problem was coronary artery disease, a significant number were patients in the same "miscellaneous" category as the patient presented here. Ablation was considered in the case Dr Herre described, but because of the nature of the aneurysm and its effect on left ventricular function, a surgical repair and resection of the aneurysm was selected. Most patients undergoing catheter ablation receive at least two shocks to the area of the arrhythmia focus. A substantial fraction receives more than two shocks, but these appear to be well tolerated. The clinical results in these patients are summarized in Table 1. In less than 20% was the ventricular tachycardia still eradicated at the time of the last follow-up visit and the patients asymptomatic off all antiarrhythmic drug treatment. Another 40% were also asymptomatic but

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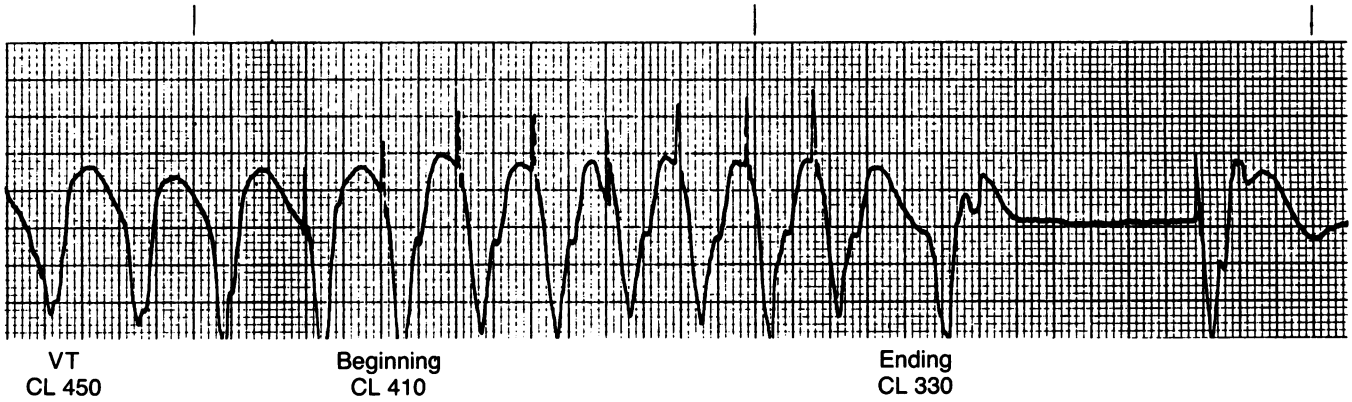

Figure 6.—This electrocardiographic strip was taken during a pacing determination of an episode of ventricular tachycardia **(VT)** of a cycle length **(CL)** of 450 ms. Pacing is initiated at a cycle length of 410 ms and decreases with each interpulse interval. By the end of the burst, the cycle length is down to 330 ms. The burst is effective, and a paced rhythm is restored.

were so only with the assistance of antiarrhythmic drugs. All of these patients had been symptomatic before the procedure because their ventricular tachycardias were not controlled when receiving the same drugs. Almost 60% of patients experienced a substantial benefit from the procedure, while 40% appeared not to have had any significant improvement. A closer examination of the patients who died during the period of follow-up shows that total cardiac mortality exceeds that of arrhythmia. These patients have advanced cardiac disease, and some die of various cardiac and noncardiac causes. There were 11 procedure-related and 16 sudden deaths in the group, presumed to have resulted from recurrent ventricular arrhythmias. So the procedure, while frequently beneficial and certainly an alternative to surgical ablation, is not a magical cure for this malignant process.

We may also take a completely different approach to the problem of sudden death through the use of device therapy for the management of these patients. At present, this might be more accurately categorized as an adjunct therapy or safety net for a more primary therapy such as drugs, surgical treatment, or ablation. Various strategies are available including arrhythmia termination, principally by defibrillation. Pacing, especially short bursts of rapid pacing, can be effective (Figure 6), but the risk of arrhythmia acceleration is substantial. Attempts to terminate a tachycardia using a burst of rapid ventricular pacing can destabilize the reentry circuit and produce a much faster and more unstable rhythm.[17] If this occurs in a patient with an implanted device, death may result. Specifically, Naccarelli and colleagues found almost 20% of patients to have arrhythmia acceleration.[17] Therefore, without an implanted defibrillator for a backup, we generally do not use automatic pacemakers in patients with ventricular arrhythmias.

Figure 7 was taken from a Holter monitor of an ambulatory patient and shows the action of the automatic implantable defibrillator in a patient with sustained ventricular tachycardia. The device is equally effective in patients with ventricular fibrillation. The present version of the implanted defibrillator is large, weighing 250 grams, and is connected to the heart using an epicardial patch electrode. On sensing ventricular tachycardia, which takes about 10 to 30 seconds, the device will deliver a sequence of four defibrillating pulses, the first of about 25 J, with three subsequent shocks of 30 J each. If the arrhythmia continues despite the delivery of these four shocks, the device becomes quiescent. It then resumes its function until after it has sensed about 30 seconds of normal rhythm. The device is triggered by the cardiac rate, and the available rate cutoffs range from 155 to 205 beats per minute. Some models also use a measure of randomness of the baseline heart rate (probability density function), which is effective for detecting ventricular fibrillation.

TABLE 2.—*Indications for Automatic Implantable Cardioverter-Defibrillator*

Failures of diagnosis
No arrhythmia inducible
No arrhythmia on monitoring
Inability to provide adequate preventive therapy
Failure of selected therapy
Clinical recurrence on class I drug therapy predicted effective by electrophysiologic study
Clinical recurrence on amiodarone therapy
Clinical recurrence after surgical or catheter ablation
Predicted high risk for failure of therapy
Inducible on the most effective class I antiarrhythmic drug
Clinical and electrophysiologic study finding predicting a high risk of failure of amiodarone therapy
Inducible after surgical or catheter ablation

Currently two methods of implanting the device are used. One uses a transvenous lead in the right ventricular apex and a defibrillating lead placed in the superior vena cava. This approach also requires at least one epicardial patch lead. An alternative is the use of patches on both the right and left ventricles and two epicardial screw-in sensing leads. This is the approach preferred at UCSF. A single incision is made in either the subxiphoid or the subcostal region, and the device is implanted in the abdominal wall. The device can also be implanted through a median sternotomy at the time of some other surgical procedure, such as revascularization or aneurysmectomy, or through a left lateral thoracotomy.[18]

When do we use the automatic implantable cardioverter-defibrillator (AICD)? The indications are divided into three categories (Table 2). The first is a failure to diagnose the cause of ventricular arrhythmias. Dr Herre referred to this when he talked about the patient who had recorded clinical ventricular arrhythmias but little ectopy on Holter monitoring and whose arrhythmia was not inducible in the electrophysiology laboratory. Depending on the cause of the heart disease, some 10% to 40% of patients have ventricular arrhythmia that is not inducible. This category of patients, those in whom there is no way to test the efficacy of therapy, are candidates for the AICD. The second group of patients

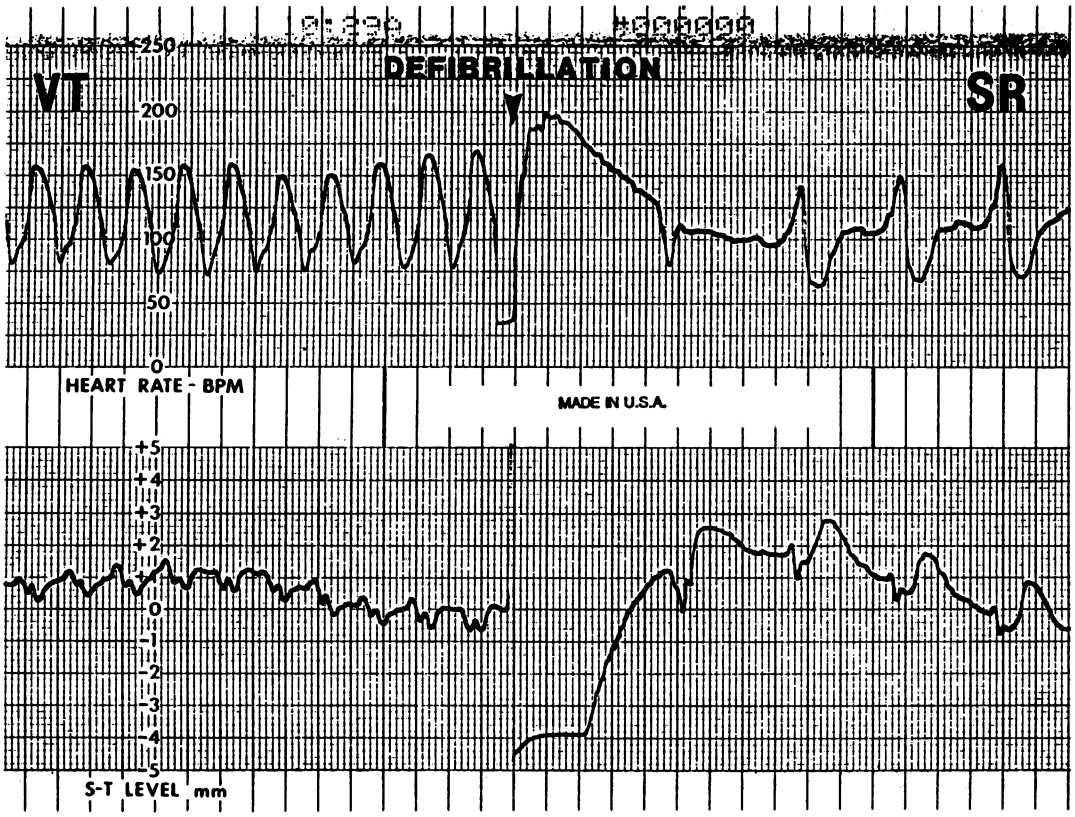

Figure 7.—This 2-channel electrocardiographic strip, taken from an ambulatory monitoring study, shows the conversion of ventricular tachycardia **(VT)** to sinus rhythm **(SR)** by a single shock from an automatic implanted defibrillator.

are those who have suffered a clinical failure of therapy with a recurrence of arrhythmia, either while taking an antiarrhythmic drug or after an operation or ablation predicted effective by electrophysiologic testing, our best predictor of therapeutic success. The final category includes those patients for whom a failure of therapy might be predicted.

We have already seen the results in patients still inducible on a regimen of class I drugs. In a study done here, we used clinical criteria to predict those patients who are at high risk despite amiodarone therapy: patients who have syncope as a presenting symptom or sudden death, those who have significant left ventricular dysfunction, and those who have persisting ventricular tachycardia on Holter monitoring after a week of amiodarone therapy.[19] An electrophysiologic study may also provide useful information about risk while on amiodarone therapy. The conversion of a hemodynamically unstable ventricular tachycardia or ventricular fibrillation to a significantly slower rhythm that is well tolerated also predicts long-term clinical success. Finally, there are those patients whose clinical arrhythmia is still inducible following surgical or ablative therapy.

Like other therapies, the AICD does not prevent progressive morbidity in these patients. They do have advanced cardiac disease, and some still die of arrhythmic and nonarrhythmic causes. What the device can do is to virtually eliminate the risk of sudden cardiac death. None of our patients have died suddenly in the first two years after implantation. As predicted from the data of Cobb and associates, empiric therapy would have resulted in an estimated 40% recurrence over the same time period.[20] Even with surgical therapy or with electrophysiologically guided drug therapy, the mortality rate is usually in the 15% to 20% range for this same time period.

There are other negatives as well. Some patients simply do not have a good psychological adjustment to this approach to arrhythmia management. A thorough discussion of the device, what it does, what it does not do, and what the expectations should be, is important in preparing patients for living with an implanted defibrillator. Patients who otherwise have a poor prognosis may not be candidates. There is a substantial morbidity, significant expense, and a small operative mortality associated with implanting the device. Finally, there are certain technical device limitations. Frequent episodes of ventricular tachycardia are not manageable with the device. First of all, the shocks are either uncomfortable—if the patient is conscious—or result in syncope. Second, the device has a limited amount of charge and a limited number of shocks that it can deliver. If the rates of ventricular tachycardia are slow and overlap with those of sinus tachycardia, unnecessary shocks may be delivered.

I will now provide a glimpse of the future. A patient was admitted to UCSF in late November 1986 with end-stage ventricular tachycardia. He had been treated unsuccessfully with eight available and investigational antiarrhythmic drugs. He had undergone a catheter ablation procedure in this hospital that was successful for a period of time in preventing the recurrence of frequent episodes, but the patient finally returned, his arrhythmia again out of control. In December 1986, he had both an AICD and an automatic tachycardia detection and terminating pacemaker implanted. In the two months after hospital discharge, he sustained 76 episodes of ventricular tachycardia, all of which were termi-

nated by the pacemaker. None of the episodes required termination by the AICD implanted in the event a pacing episode produced acceleration. The patient has continued to have ventricular tachycardia with a similar frequency, but after two years of follow-up the implanted defibrillator has been required on only one occasion. At present, the pacemaker has terminated nearly 1,000 episodes of tachycardia. We hope that in the near future we will have the capabilities of both these devices in a single pacemaker-defibrillator. At that time, the device therapy for ventricular arrhythmias can truly move into the realm of treatment rather than simply serving as a safety net.

Questions and Answers

PHYSICIAN IN THE AUDIENCE: *I have two questions regarding the paper on electrophysiologic study after myocardial infarction: First, were those patients evaluated by other known predictors of mortality after myocardial infarction, left ventricular dysfunction, and ventricular ectopic beats? Second, were they preselected as high-risk patients?*

DR HERRE: No, they were not preselected as high-risk patients. The study was a consecutive series of 175 patients. The finding of left ventricular dysfunction identified some of the same patients and some different patients as at increased risk of mortality. Ambulatory monitoring was not done in that particular study, but other studies where ambulatory monitoring has been used show that it takes a very large number of subjects to show statistically significant indices of an increased risk of mortality. So these two methods are still valid for stratifying patients following myocardial infarction. It appears that an electrophysiologic assessment may be more specific but, as you may recall, there were three studies that showed virtually no difference. The jury is still out on the value of electrophysiologic study in the postmyocardial infarction period.

PHYSICIAN IN THE AUDIENCE: *You indicated that an electrophysiologic study for patients with recurrent syncope of an unknown origin yielded about 20% diagnosable findings. Clinically speaking, how do you reconcile the separate data you mentioned earlier that in patients who have no clinical ventricular tachycardia you encounter about 2% to 10% of sustained nonclinical ventricular tachycardia—that is, a false-positive finding, depending on the number of extrastimuli used?*

DR HERRE: If you are doing a study for syncope, the end point and the interpretation of the data are a little different. A diagnostic test is one that induces a sustained arrhythmia or bradyarrhythmia, something that could have caused the patient's syncope without leading to a cardiac arrest. The nonclinical arrhythmias induced in an electrophysiologic laboratory are generally very fast, are frequently polymorphic, and frequently lead to ventricular fibrillation. The arrhythmia that we are looking for is somewhat slower, is unimorphic, and is stable. We think that we have come up with an answer that is useful in about 20% of cases.

PHYSICIAN IN THE AUDIENCE: *What are the relative costs of the different therapies?*

DR GRIFFIN: Amiodarone costs $1.50 a pill. Most patients take two pills a day, so the cost is about $100 a month. Even with follow-up visits about every six months that include a cardiogram, some lab work, and a chest radiograph, the total cost is pretty inexpensive. The cost of an electrophysiologic study is $3,000 or more. The hospital stay itself may be anywhere from a couple of days to a couple of weeks, and it is not cheap. The minimum cost of an AICD is about $25,000. The addition of an antitachycardia pacemaker costs another $10,000 and that, too, requires a couple of weeks in hospital. The cost of an arrhythmia operation is in the range of $25,000 to $40,000. So, all in all, amiodarone therapy is far cheaper than any of the things that we have talked about. Most of the methods that we talked about using are applied in patients in whom either intolerable side effects have developed or who have failed amiodarone therapy. We have few patients with defibrillators who do not fall into one of those categories. About 5% of the patients we see for ventricular arrhythmias end up with a defibrillator. So these are carefully selected patients who really do not respond to anything else.

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